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Abstract: Arginine vasopressin (AVP) is an important hormone for osmoregulation, while as a neuropeptide in the brain it plays an important role in the regulation of social behaviors. Dry habitats are often the home of obligately sociable species such as meerkats and Damaraland mole-rats, leading to the hypothesis that high plasma AVP levels needed for osmoregulation might be associated with the regulation of social behavior. We tested this in a facultative sociable species, the African striped mouse (Rhabdomys pumilio). During the moist breeding season, both solitary- and group-living reproductive tactics occur in this species, which is obligatory sociable in the dry season. We collected 196 plasma samples from striped mice following different reproductive tactics both during the moist and the dry season. Solitary mice did not have lower AVP levels than sociable mice, rejecting the hypothesis that peripheral AVP is involved in the regulation of alternative reproductive tactics. However, we found significantly higher AVP levels during the dry season, with AVP levels correlated with the abundance of food plants, the main source of water for striped mice. Plasma AVP levels were not correlated with testosterone or corticosterone levels. Our study underlines the important role that AVP plays in osmoregulation, particularly for a free ranging mammal living under harsh arid conditions.

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Arginine vasopressin plasma levels change seasonally in African striped mice but do not differ between alternative reproductive tactics

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Abstract

Arginine vasopressin (AVP) is an important hormone for osmoregulation, while as a neuropeptide in the brain it plays an important role in the regulation of social behaviours. Dry habitats are often the home of obligately sociable species such as meerkats and Damaraland mole-rats, leading to the hypothesis that high plasma AVP levels needed for osmoregulation might be associated with the regulation of social behaviour. We tested this in a facultative sociable species, the African striped mouse (*Rhabdomys pumilio*). During the moist breeding season, both solitary- and group-living reproductive tactics occur in this species, which is obligatory sociable in the dry season. We collected 196 plasma samples from striped mice following different reproductive tactics both during the moist and the dry season. Solitary mice did not have lower AVP levels than sociable mice, rejecting the hypothesis that peripheral AVP is involved in the regulation of alternative reproductive tactics. However, we found significantly higher AVP levels during the dry season, with AVP levels correlated with the abundance of food plants, the main source of water for striped mice. Plasma AVP levels were not correlated with testosterone or corsticosterone levels. Our study underlines the important role that AVP plays in osmoregulation, particularly for a free ranging mammal living under harsh arid conditions.

Keywords: social flexibility, communal breeding, cooperative breeding, intra-specific variation, social organization, vasopressin, drought, helper

1. Introduction

Hormones are potent modulators of social behaviour but they also have significant physiological functions. Experimental manipulation of testosterone can influence sexual and reproductive behaviour as well as reproductive physiology [44]. Glucocorticoids can influence social behaviour and also play a key role in metabolism, including emergency-life history stages [21]. The peptide hormone prolactin plays a significant role in the regulation of parental care in both sexes, but also influences osmoregulation, growth, immunology and reproductive physiology [26]. However, while the dual function of hormones in regulating behaviour and physiology is well known, studies in behavioural endocrinology often ignore the physiological function of hormones.

The neuropeptide arginine vasopressin is produced in the brain, where its secretion in different brain areas influences several social behaviours like parental care, pair bonding and aggression [8, 9]. Produced in the paraventricular nucleus (PVN) and secreted via the pituitary into the blood stream, it plays an important role in osmoregulation [5]. Dehydration increases AVP secretion, which then acts on the kidneys where it triggers the contraction of arterioles in the glomeruli and reabsorption of water from the collecting ducts, decreasing water loss and increasing blood pressure [5]. Traditionally, it has been assumed that AVP secretion in the brain (influencing behaviour) is independent from AVP secretion by the pituitary (influencing osmoregulation) [10]. Several studies have suggested that nasally administrated AVP can pass through the blood-brain barrier [4], leading to significant behavioural effects in humans and animals [3, 4, 39]. However, this has been recently criticized and it has been argued that putting AVP into the nasal cavity is simply a convenient way to get it into the blood supply, indicating that peripheral AVP can

cross the blood-brain barrier [20] and could then influence behaviour via actions in the brain. This criticism has been supported by studies showing that peripheral administration of AVP and the closely related oxytocin had significant effects on social behaviour [13, 14]. This leads to the hypothesis that peripheral levels of neuropeptides might influence social behaviour via central effects. Additionally, peripheral levels of AVP could influence behaviour via peripheral effects such as changes in blood pressure and heart rate [19].

The relationships between AVP and steroid hormones are complex (reviewed by [8]). The AVP receptor 1b is expressed in cells producing adrenocorticotropin in the anterior pituitary [2]. Further, AVP is produced in the PVN, which also synthesizes corticotrophin releasing hormone (CRH). AVP from the suprachiasmatic nucleus has been reported to regulate CRH and ACTH secretion from the pituitary [6]. Finally, AVP is secreted from the PVN in response to stress [1, 45]. Another steroid hormone that influences AVP is testosterone [12]. Experimental testosterone administration increases the density of AVP fibres within the lateral septum [40], while gonadectomy reduces AVP in brain areas connected to the basal nucleus stria terminalis and the medial amygdala, [41, 42]. Based on these studies, peripheral AVP can be expected to correlate with corticosterone while it is at present not clear whether peripheral AVP might also correlated with testosterone.

AVP is an important modulator of social behaviour, but its traditional physiological function is in osmoregulation [5, 8]. Interestingly, arid areas, in which it is necessary to increase AVP secretion to reduce water loss, often are host to especially sociable species such as meerkats, Damaraland mole rats and naked mole rats [11, 17]. In prairie voles, peripheral AVP injection positively influences the formation of pair bonds only in males from dry areas but not from moist areas [14].

This may suggest that the environmental regulation of AVP secretion in response to water shortage could have a positive influence on sociality. In other words, the evolution of group-living in dry habitats might have been associated with environmentally induced AVP secretion.

The African striped mouse (*Rhabdomys pumilio*) in the Succulent Karoo semi-desert of South Africa is obligatory group-living during the dry hot season, which is characterized by both food and water shortage [31]. However, this species shows high social flexibility during the moist and cold breeding season in spring [30]. Specifically, depending on population density, striped mice can either live solitarily, in small or in extended family groups [28]. Individuals of both sexes can adopt three alternative reproductive tactics [30]: 1. remain as non-breeding adult philopatric helpers at the nest; 2. disperse and become a solitary breeder (roaming males; solitary breeding females); or 3. communal breeding of females with one group-living breeding male. However, when the breeding season terminates and the hot dry non-breeding season begins, all striped mice become highly sociable and form groups: roamers will join solitary breeding females, while offspring will remain philopatric, staying with their mother long-after reaching adulthood, leading to the formation of family groups. It is therefore possible that an environmentally induced increase in AVP secretion at the end of the breeding season in response to increasing drought is a proximate cause of social change in this species. Laboratory studies have shown that solitarily-kept males do not differ in AVP receptor expression in different brain areas, making it likely that their brains are as responsive to AVP secretion as those of group-living males [36]. It has also been shown that solitary kept males have more AVP stored in their PVN than group-living males [27]. Thus, solitary males might be able

to change their social behaviour by increasing their AVP secretion, which could be induced by water scarcity due to increased drought at the beginning of the dry season.

In the present study we compared AVP levels during the breeding season in male and female African striped mice exhibiting alternative reproductive tactics. First, we predicted AVP levels to be higher in the dry season than in the moist breeding season, due to its important effect on osmoregulation. Second, if plasma AVP plays an important role in the regulation of social behaviour, we expected significant differences between individuals following different tactics. Specifically we predicted solitary-living roaming males to have significantly lower AVP levels than group-living ones. We focused on males, as during the study few solitary breeding females were present at the field site. Third, as AVP has been reported to be stress reactive and testosterone dependent, we tested for significant correlations between AVP and the steroid hormones corticosterone and testosterone.

2. Materials and Methods

2.1.Study species

Striped mice breed in the austral spring (August/September to November/December; [32] and most individuals born during the breeding season remain philopatric as young adults (>6 weeks old) in their natal group, where they remain for the duration of the entire dry season (December-April) and the cold wet winter (May-July), reaching independent breeding status only the following spring. Typically, males will then disperse and attempt to immigrate into groups of communally breeding females, while females will remain in their group and breed communally. However, both sexes

can also breed solitarily and individuals can leave their group at a young age of 4-6 weeks if free territories are available [22], but often only leave when 1 year old in the next breeding season [28]. Group-living breeding males represent the bourgeois tactic with the highest reproductive success, philopatric males have the lowest reproductive success, while solitary-living roamers have low success when population density is high, but similar success to territorial breeders when population density is low [29]. It is important to note that some philopatrics may also be successful in reproducing [29], a phenomenon that has been also reported for helping males in other species [16, 47].

2.2.Study area

The study was conducted in Goegap Nature Reserve in South Africa (S 29 41.56, E 18 1.60). Goegap lies within the semi-desert biome of the Succulent Karoo, which is characterized by cold and moist winters followed by spring with high food abundance and hot dry summers. In spring, the landscape is dominated by short-living ephemerals, which typically give way to succulent shrubs in summer. Blood samples were collected during the breeding season 2011 (September, October and November) and the following dry season in 2012 (January and February).

2.3.Plant surveys

Striped mice obtain their water from their food plants; in the Succulent Karoo both succulents and ephemerals (wildflowers) are important sources of water. Plant surveys were carried out on the 15th of each month on monitoring plots located within the home-ranges of eight different groups. Each plot covered an area of 2 x 2 m and was sampled using standard protocols (the Braun-Blanquet Method [43] which was also employed in previousl studies on striped mice [34]). In brief, we recorded the number

and palatability of each food plant contained within each monitoring plot (palatability know from behavioural observations [34]). Of all the plants recorded, only short-living plants with high water content such as ephemerals and succulents were included for analysis for this study. As a measure of food and thus water availability we took the mean of the eight plots for each month we collected blood samples.

2.4.Determination of reproductive tactics

Reproductive tactics were determined by a combination of trapping, behavioural observations and radio-tracking. All methods followed well established protocols used successfully in striped mice studies since 2001. Trapping was be done around striped mice nesting sites. Each site was trapped regularly at least three days per month. Trapped striped mice were weighed, sexed, and permanently marked with ear tags (National Band and Tag Co., USA) and temporarily with hair dye (Inecto Rapido, Pinetown, South Africa) to facilitate individual recognition during behavioural observations [23, 31]. All solitary-living individuals and 1 to 4 striped mice from each group were fitted with radio-collars (Holohil, Canada) and were radio-tracked to determine sleeping sites locations [33, 34]. Carrying a radio-collar does not significantly affect either corticosterone levels or behaviour in striped mice [25]. Mice that were trapped at a nest as juveniles (body mass <30g) and trapped there subsequently, were regarded as philopatrics. Females that showed signs of breeding (lactating nipples, open vagina and loss of body mass indicating parturition, or high body mass indicating pregnancy), were regarded as breeding females. Large heavy males that left their natal group and immigrated into a group of communally breeding females were considered as breeding males. Males and females that left their natal group and slept alone were regarded as roaming males or solitary breeding females.

2.5.Blood sampling

Altogether, we collected 196 plasma samples from68 females and 64 males (some individuals were sampled more than once; for sample sizes of the different social categories see Fig. 1). Mice were trapped at their nests during the morning shortly after they became active to control for possible circadian rhythms of hormone secretion. Traps were watched from a distance of 10m and, as soon as a mouse entered a trap, it was taken out and anaesthetized with di-ethyl ether [25]. A blood sample of about 300µl was obtained from a sub-lingual vein, a less harmful method than traditionally used techniques of blood sampling [18]. Each sample was taken within 2-3min to avoid a stress response [25]. Samples were collected in a cold tube containing EDTA, which were kept in the field on ice before being centrifuged in a fridge at the research station. Samples were stored at – 20 °C at the research station and transported to Zurich on dry ice for processing.

2.6.Hormone assays

We used the commercial EAI kit ADI-901-017 for Arginine-Vasopressin from Enzo Life Sciences. Cross reactivity with other hormones was <0.001%, as stated in the manual. Samples were diluted with an assay buffer by 1:3. Serial dilution of striped mouse plasma from 1:1 to 1:9 paralleled the standard curve. Intra-assay coefficient of variation for seven samples from one pool of striped mouse plasma was 14.2%. Inter-assay coefficients of variation for two pools of striped mouse plasma (each five samples) were 16.7% and 12.1%. From 111 of the 196 samples, we also measured testosterone and levels, and from 112 samples we also measured corsticosterone levels (mostly the same as samples as used for testosterone). For this we used

commercial kits from IBL Hamburg, which were previously validated for striped mouse serum [24]. Procedures were as stated in the kit manuals, but due to high corticosterone levels typical of this species, samples were diluted 1:99. All measurements were well within the standard curve of the assay. Intra- and inter-assay variability was determined with pools from striped mice and were all below 10%.

2.7.Data analysis

We used the statistical software R (version 2.11.0 R Development Core Team 2006) to perform all analyses. AVP was log-transformed, such that residuals followed a normal distribution (confirmed by visual inspection of normality plots). All data are presented as mean + SEM. We used linear mixed effect models (LMMs) to determine whether AVP levels were influenced by 1) social tactics during the breeding season; 2) season and the interaction between season and tactics (by comparing AVP levels of group-living individuals between seasons) 3) food; 4) testosterone; and 5) corsticosterone. As some individuals were measured more than once, individual ID was included as the random factor in each model. As the sexes can differ significantly in both corsticosterone and testosterone values [25], models 4 and 5 were done separately for each sex.

3. Results

3.1.Seasonal changes in AVP levels

AVP levels were significantly influenced by season (LMM: $F_{1,45} = 11.79$; $p = 0.001$), while the interaction between social tactics and season was not significant (LMM:

$F_{2,45}$ = 2.31; p =0.11; Fig. 1). Further analysis of pairwise comparisons using LMM revealed significantly higher AVP levels during the dry season in philopatric females (LMM: F1,32 = 8.29; p =0.007), and breeding females (LMM: F1,18 = 10.00; p =0.005), with a trend in philopatric males (LMM: F1,4 = 5.96; p =0.07), and no significant effect in breeding males (LMM: F1,14 = 0.18; p =0.67). AVP significantly increased when less food plants were available (LMM: $F_{1,61}$ = 20.09; p < 0.0001; Fig. 2).

3.2.Differences in AVP levels between ARTs

We found no significant difference in AVP levels among male (LMM: $F_{1,24}$ = 3.07; p = 0.09; Fig 1) and female alternative reproductive tactics (LMM: $F_{1,19}$ = 0.64; p = 0.43; Fig 1).

3.3.Correlations between AVP and steroid hormones

In females AVP levels did not correlate significantly with corticosterone levels (LMM: $F_{1,7}$ = 1.30; p = 0.29; Fig. 3a) nor with testosterone levels (LMM: $F_{1,7}$ = 0.65; p = 0.65; Fig. 3b). In males AVP levels did not correlate significantly with corticosterone levels (LMM: $F_{1,25}$ = 0.130; p = 0.73; Fig. 3a) nor with testosterone levels (LMM: $F_{1,25}$ = 0.16; p = 0.69; Fig. 3b). Males had significantly higher testosterone levels in the breeding compared to the dry season (3.3 $\pm$ 0.4ng/ml versus 1.1 $\pm$ 0.2 ng/ml, LMM: $F_{1,17}$ = 13.62; p = 0.002).

4. Discussion

We found a significant increase of plasma AVP levels during the dry season but no difference in AVP level among reproductive tactics. AVP levels correlated with the

availability of water storing food plants, but were not related to steroid hormone concentrations. Therefore, the major role of peripheral AVP seems to be in osmoregulation, but not in the regulation of reproductive tactics and sociality.

In laboratory rats, dehydration increases AVP secretion, which then acts on the kidneys where it triggers the contraction of arterioles in the glomeruli and reabsorption of water from the collecting ducts, decreasing water loss and increasing blood pressure [5]. While it is believed that AVP plays a significant role in osmoregulation in small desert mammals [37], few studies have directly measured AVP in free ranging animals. Studies on spiny mice (*Acomys spec.*) from the deserts of Israel found that peripheral administration of AVP inhibits reproduction [38, 46]. These studies assumed that spiny mice showed an increase of AVP levels under water stress, but to our knowledge, peripheral AVP had not been measured in free ranging spiny mice. Ours is one of the first field studies measuring peripheral AVP in a desert mammal, providing empirical evidence for the general assumption that AVP increases during dry seasons. This is important basic knowledge for research programs on how natural populations can cope with droughts, a phenomenon that is predicted to occur more often in the future as a consequence of global warming [15].

Numerous studies demonstrated a relationship between AVP and both glucocorticoids and testosterone, even though these relationships are complex (reviewed by [8]). Both corsticosterone and AVP are stress responsive [1, 45], but in our present study we found no significant correlation between AVP and corsticosterone. In spiny mice, gonadal activity is regulated by AVP, and experimentally increasing AVP (mimicking the predicted AVP increase under water stress) decreases testosterone levels and testis mass [7]. Testosterone can influence brain AVP levels directly [12] and AVP plays a significant role in the seasonal

regulation of reproduction in spiny mice [46]. We found a significant seasonal decrease in male testosterone levels in the present study, which is in accordance with previous findings [25], and at the same time a seasonal increase of AVP levels. However, there was no significant correlation between AVP and testosterone.

Male striped mice following ARTs have different levels of steroid hormones (both corticosterone and testosterone) and of the peptide hormone prolactin [24, 25, 35]. Additionally, these hormones change seasonally, with a decrease during the dry season [24, 25, 35]. Given the significant role of AVP in the regulation of social behaviour in microtine rodents (reviewed by [8]) and the indication that peripheral AVP might influence social behaviour [13, 14, 19, 20], we tested the hypothesis that peripheral AVP levels differ between ARTs in striped mice. Specifically, we predicted solitary roamers, which do not engage in social bonding, to have lower AVP levels. However, we did not find any differences between ARTs, and the AVP levels of solitary roamers (and the few solitary females we could sample) were similar to the ones of striped mice following a sociable tactic. In the brain, roamers have higher levels of stored AVP than group-living males [27] while their brains have as many AVP receptors as sociable males [36]. Roamers might thus be able to release AVP in the brain to form social bonds, should they immigrate into a group and become group-living [36]. Therefore, our study on peripheral AVP does not exclude the possibility that AVP as a neuropeptide in the brain modulates social behaviours. Thus, while plasma AVP does not seem to play a role in the regulation of ARTs during the breeding season, the possibility that the environmental regulation of peripheral AVP secretion in response to water shortage could have a positive influence on sociality cannot be ruled out. Striped mice, meerkats and Damaraland mole-rats are highly sociable in dry environments [11, 17] which are thought to induce high AVP levels. It

would be interesting to compare plasma AVP levels of sociable desert mammals with those of non-sociable ones, or to test the behavioural responses of striped mice to AVP injection during the moist season, as was done in prairie voles [14].

5. Conclusions

This is one of the first field studies showing that plasma AVP levels increase during the dry season and are negatively correlated with the availability of water-providing food plants. This highlights the important role of AVP in osmoregulation in wild animals, especially in arid habitats. While it has been previously shown that other hormones, such as corsticosterone and testosterone also change seasonally, we found no significant correlation between them and AVP, suggesting that the secretion of steroid hormones is independently regulated from AVP secretion. We further found no evidence that plasma AVP levels are related to social behaviour, which suggests that the physiological role of AVP in osmoregulation might be disconnected from its role as a behavioural mediator in the brain.

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Figure captions

Fig. 1

AVP plasma levels of striped mice belonging to different social categories (solitary roamers; BM = breeding males; PhilM = philopatric males; Solit F = solitary breeding females; BF = comunally breeding females; PhilF = philopatric females) during different seasons (white: moist breeding season; black: dry season). Note: solitary mice marked in striped bars (roamer males and Solit F) only occur during the breeding, but not during the dry season. Mean $\pm$ SEM and sample sizes are shown.

Fig. 2

Correlation between AVP plasma levels and food availability measured in monitoring plots of 4 square metres. Samples were collected during 5 months differing in food availaility (3 months in the moist breeding season and 2 months of the dry season), so each of the five different food values represent one month.

Fig. 3

(a) Correlations between AVP plasma levels and corticosterone levels were non-significant for both females ($p=0.29$) and males ($p=0.73$). (b) Correlations between AVP plasma levels and testosterone levels were non-significant for both females ($p=0.65$) and males ($p=0.69$).

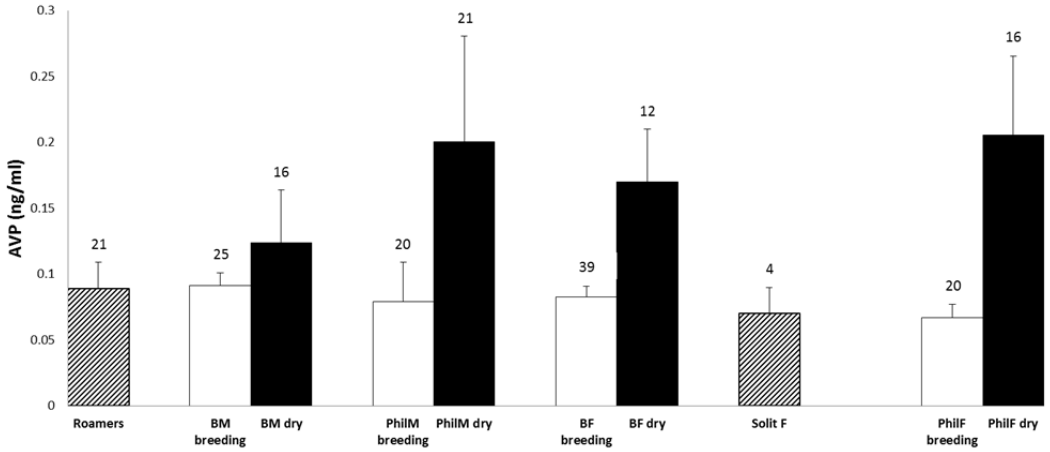

AVP (ng/ml)
0.3
0.25
0.2
0.15
0.1
0.05
0
21
25
16
20
21
39
12
4
20
16
Roamers
BM breeding
BM dry
PhilM breeding
PhilM dry
BF breeding
BF dry
Solit F
PhilF breeding
PhilF dry

Fig. 1

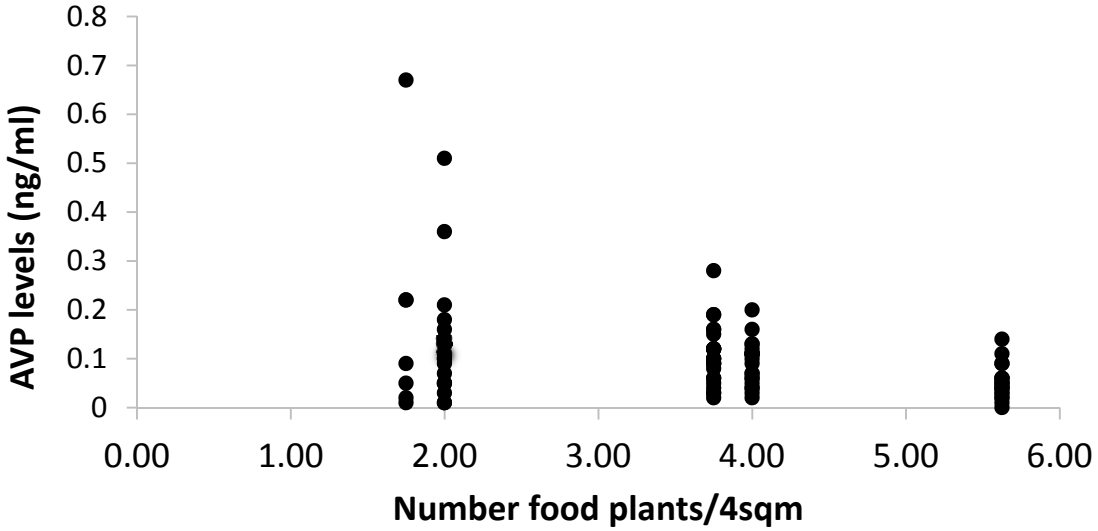
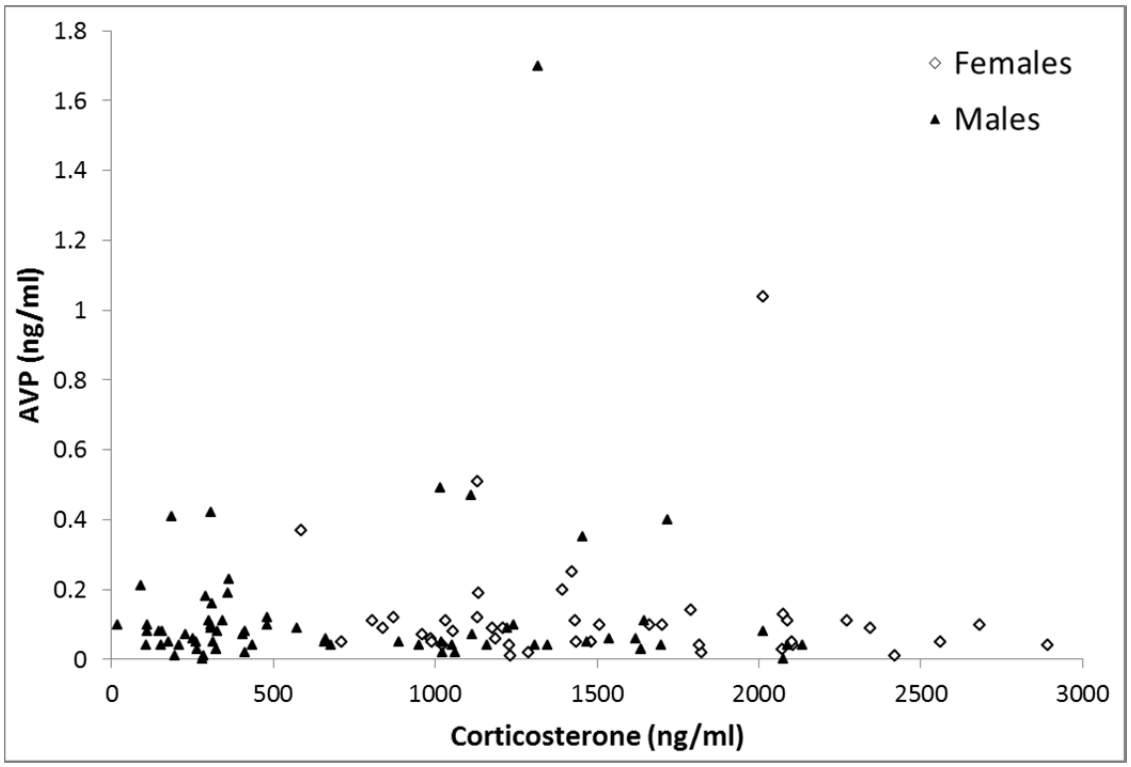
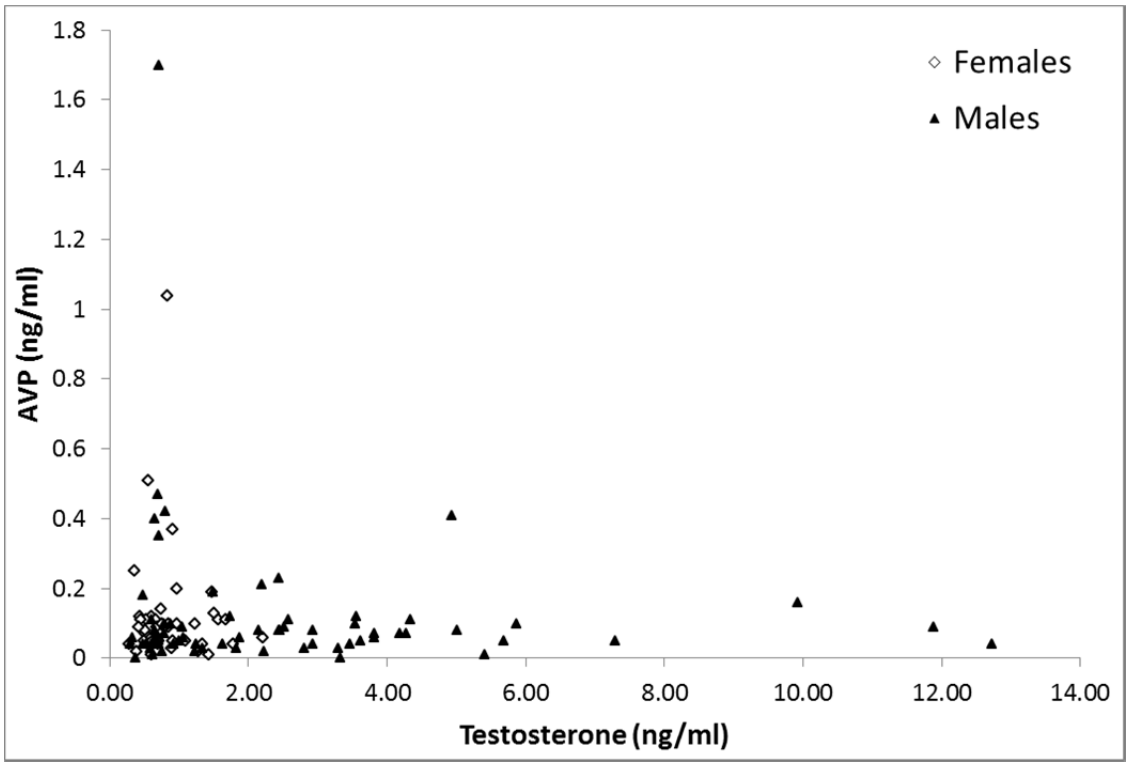

AVP levels (ng/ml)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.00
1.00
2.00
3.00
4.00
5.00
6.00
Number food plants/4sqm

Fig. 2


Females
Males
AVP (ng/ml)
Corticosterone (ng/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
0
500
1000
1500
2000
2500
3000

(a)


Females
Males
AVP (ng/ml)
Testosterone (ng/ml)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00

(b)

Fig. 3